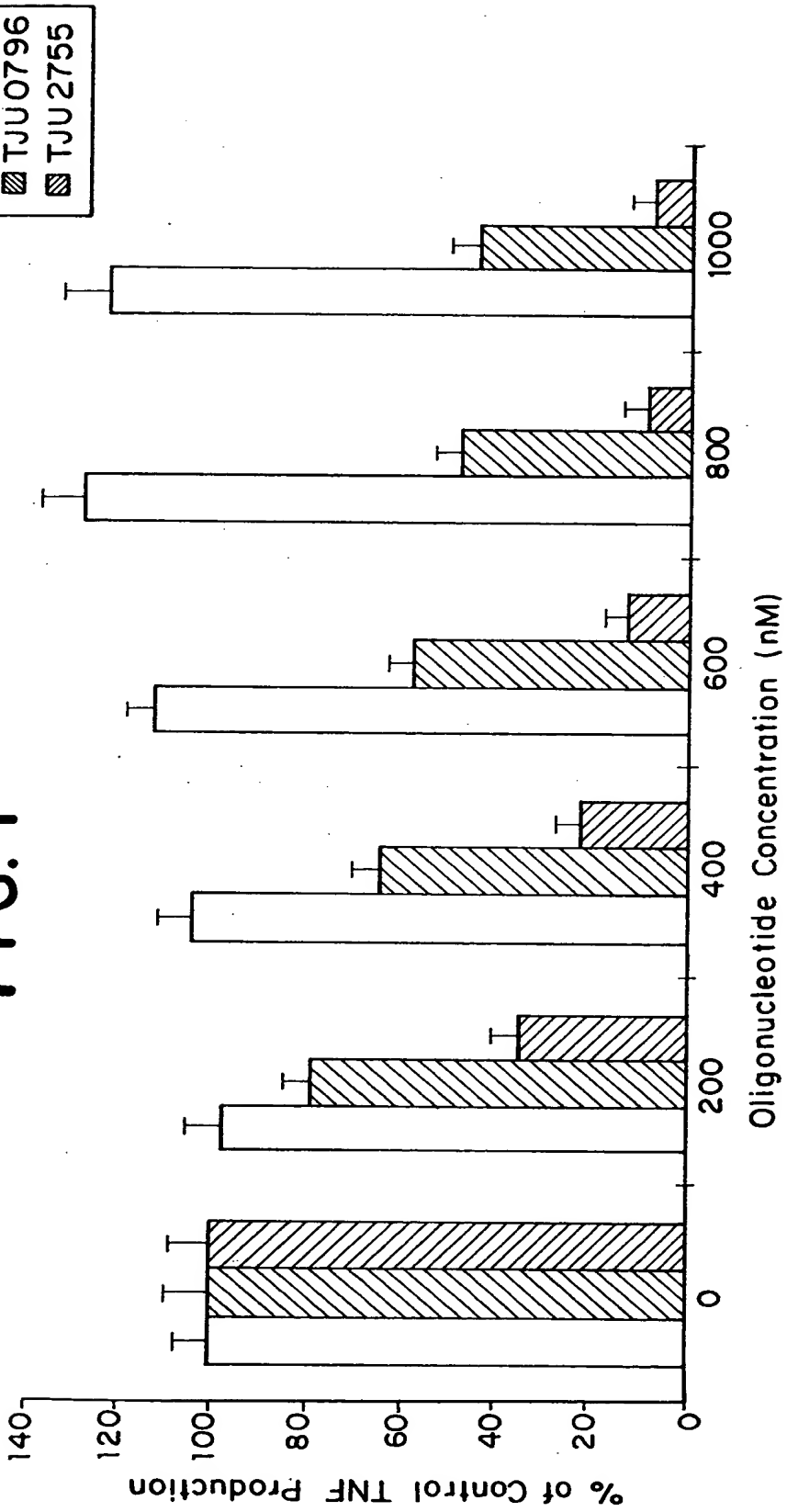
FIG. 1


TJU2826
TJU0796
TJU2755
% of Control TNF Production
0
20
40
60
80
100
120
140
0
200
400
600
800
1000
Oligonucleotide Concentration (nM)

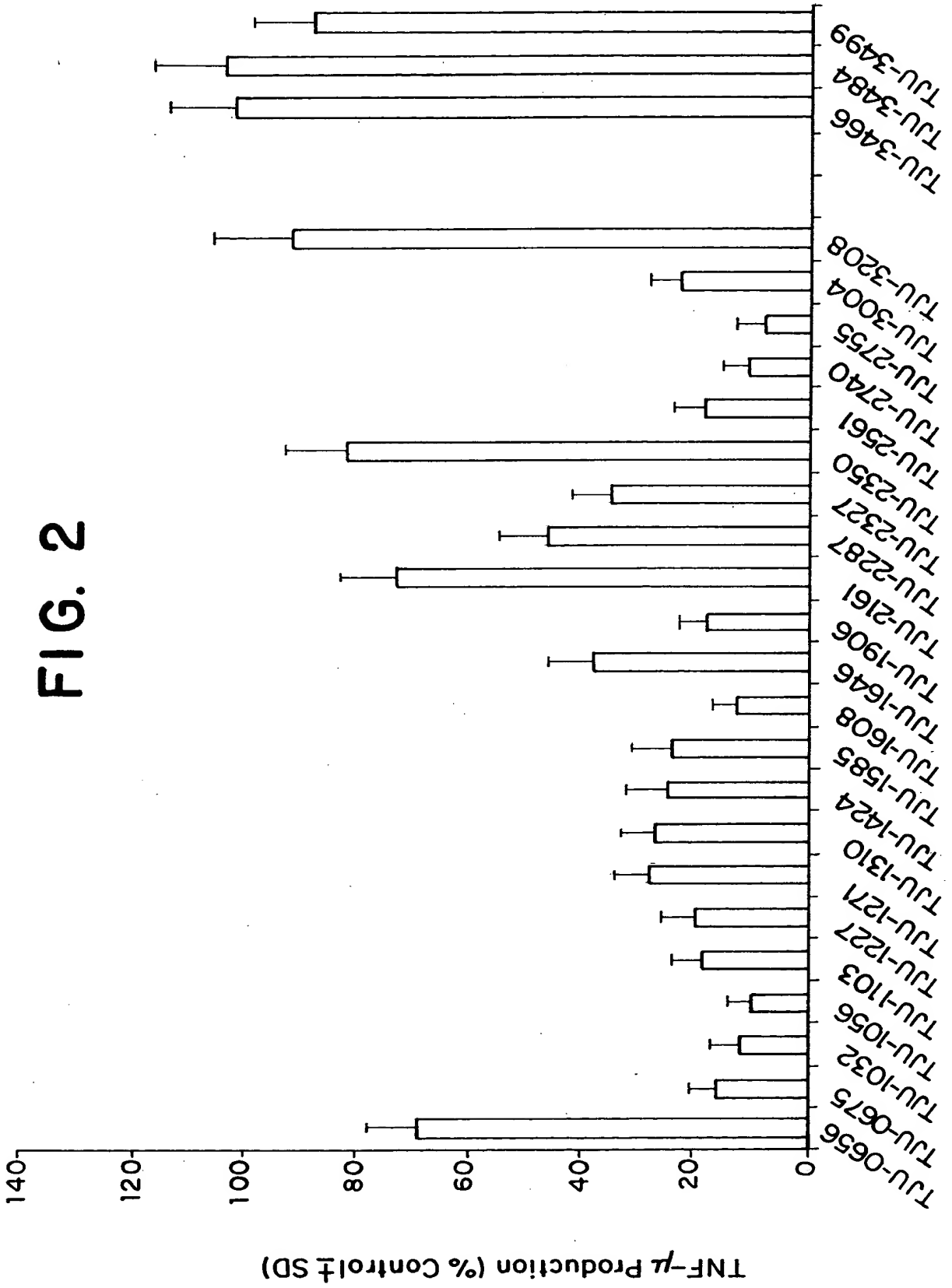
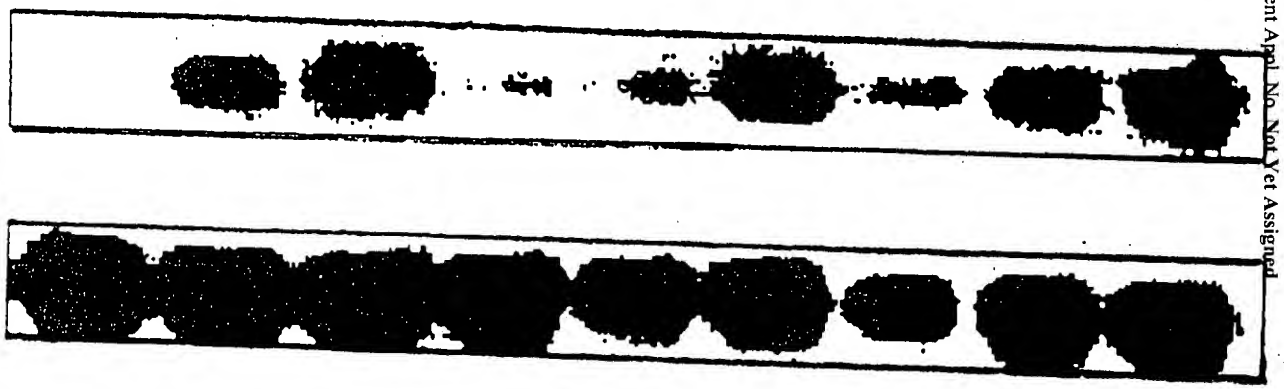

TNF-μ Production (% Control ± SD)
0
20
40
60
80
100
120
140
TJU-0656
TJU-0675
TJU-1032
TJU-1056
TJU-1103
TJU-1227
TJU-1271
TJU-1310
TJU-1424
TJU-1585
TJU-1608
TJU-1646
TJU-1906
TJU-2161
TJU-2287
TJU-2327
TJU-2350
TJU-2561
TJU-2740
TJU-2755
TJU-3004
TJU-3208
TJU-3466
TJU-3484
TJU-3499

FIG. 2

FIGURE 3

	1	2	3	4	5	6	7	8	9
Name of ASO	-	-	0796	2755	1906	2350	3004	3208	3466
Motif containing	-	-	No	Yes	Yes	Yes	Yes	Yes	Yes
LPS stimulation	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
TNF-α inhibition	-	-	48%	92%	80%	18%	77%	8%	No



```
   1 gaattccggg tgatttcact cccggctgtc caggcttgtc ctgctacccc acccagcctt
  61 tcctgaggcc tcaagcctgc caccaagccc ccagctcctt ctccccgcag gacccaaaca
 121 caggcctcag gactcaacac agcttttccc tccaacccgt tttctctccc tcaacggact
 181 cagctttctg aagcccctcc cagttctagt tctatctttt tcctgcatcc tgtctggaag
 241 ttagaaggaa acagaccaca gacctggtcc ccaaaagaaa tggaggcaat aggttttgag
 301 gggcatgGGG Acggggttca gcctccaggg tcctacacac aaatcagtca gtggcccaga
 361 agaccccccct cggaatcgga gcaGGGAgga tgGGGAgtgt gaggggtatc cttgatgctt
 421 gtgtgtcccc aactttccaa atccccgccc ccgcgatgga gaagaaaccg agacagaagg
 481 tgcagggccc actaccgctt cctccagatg agctcatggg tttctccacc aaggaagttt
 541 tccgctggtt gaatgattct ttccccgccc tcctctcgcc ccaGGGAcat ataaaggcag
 601 ttgttggcac acccagccag cagacgctcc ctcagcaagg acagcagagg accagctaag
 661 aGGGAgagaa gcaactacag acccccccctg aaaacaaccc tcagacgcca catcccctga
 721 caagctgcca ggcaggttct cttcctctca catactgacc cacggcttca ccctctctcc
 781 cctggaaagg acaccatgag cactgaaagc atgatccGGG Acgtggagct ggccgaggag
 841 gcgctcccca agaagacagg ggggccccag ggctccaggc ggtgcttgtt cctcagcctc
 901 ttctccttcc tgatcgtggc aggcgccacc acgctcttct gcctgctgca ctttggagtg
 961 atcggccccc agaGGGAaga ggtgagtgcc tggccagcct tcatccactc tcccacccaa
1021 gGGGAaatga gagacgcaag agaGGGAgag agatGGGAtg ggtgaaagat gtgcgctgat
1081 aGGGAGGGAt gagagagaaa aaaacatgga gaaagacgGG GAtgcagaaa gagatgtggc
1141 aagagatgGG GAagagagag agagaaagat ggagagacag gatgtctggc acatggaagg
1201 tgctcactaa gtgtgtatgg agtgaatgaa tgaatgaatg aatgaacaag cagatatata
1261 aataagatat ggagacagat gtggggtgtg agaagagaga tggGGGAaga aacaagtgat
1321 atgaataaag atggtgagac agaaagagcG GGAaatatga cagctaagga gagagatggg
1381 ggagataagg agagaagaag atagggtgtc tggcacacag aagacactca GGGAaagagc
1441 tgttgaatgc tggaaggtga atacacagat gaatggagag agaaaaccag acacctcagg
1501 gctaagagcg caggccagac aggcagccag ctgttcctcc tttaagggtg actccctcga
1561 tgttaaccat tctccttctc cccaacagtt ccccaGGGAc ctctctctaa tcagccctct
```

Fig. 4A

1621 ggcccaggca gtcagtaagt gtctccaaac ctctttccta attctgggtt tgggtttggg
1681 ggtagggtta gtaccggtat ggaagcagtg gGGGAaattt aaagttttgg tcttggGGGA
1741 ggatggatgg aggtgaaagt agggggggtat tttctaggaa gtttaagggt ctcagctttt
1801 tcttttctct ctcctcttca ggatcatctt ctcgaacccc gagtgacaag cctgtagccc
1861 atgttgtagg taagagctct gaggatgtgt cttggaactt ggagggctag gatttgGGGA
1921 ttgaagcccg gctgatggta ggcagaactt ggagacaatg tgagaaggac tcgctgagct
1981 caaGGGAagg gtggaggaac agcacaggcc ttagtGGGAt actcagaacg tcatggccag
2041 gtGGGAtgtG GGAtgacaga cagagaggac aggaaccgga tgtggggtgg gcagagctcg
2101 agggccagga tgtggagagt gaaccgacat ggccacactg actctcctct ccctctctcc
2161 ctccctccag caaaccctca agctgagggg cagctccagt ggctgaaccg ccgggccaat
2221 gccctcctgg ccaatggcgt ggagctgaga gataaccagc tggtggtgcc atcagagggc
2281 ctgtacctca tctactccca ggtcctcttc aagggccaag gctgcccctc cacccatgtg
2341 ctcctcaccc acaccatcag ccgcatcgcc gtctcctacc agaccaaggt caacctcctc
2401 tctgccatca agagcccctg ccagaGGGAg accccagagg gggctgaggc caagccctgg
2461 tatgagccca tctatctGGG Aggggtcttc cagctggaga agggtgaccg actcagcgct
2521 gagatcaatc ggcccgacta tctcgacttt gccgagtctg ggcaggtcta ctttGGGAtc
2581 attgccctgt gaggaggacg aacatccaac cttcccaaac gcctcccctg ccccaatccc
2641 tttattaccc cctccttcag acaccctcaa cctcttctgg ctcaaaaaga gaattggggg
2701 cttagggtcg gaacccaagc ttagaacttt aagcaacaag accaccactt cgaaacctgg
2761 gattcaggaa tgtgtggcct gcacagtgaa gtgctggcaa ccactaagaa ttcaaactgg
2821 ggcctccaga actcactggg gcctacagct ttgatccctg acatctggaa tctggagacc
2881 aGGGAgcctt tggttctggc cagaatgctg caggacttga gaagacctca cctagaaatt
2941 gacacaagtg gaccttaggc cttcctctct ccagatgttt ccagacttcc ttgagacacg
3001 gagcccagcc ctccccatgg agccagctcc ctctatttat gtttgcactt gtgattattt
3061 attatttatt tattatttat ttatttacag atgaatgtat ttatttGGGA gaccggggta
3121 tcctggGGGA cccaatgtag gagctgcctt ggctcagaca tgttttccgt gaaaacggag
3181 ctgaacaata ggctgttccc atgtagcccc ctggcctctg tgccttcttt tgattatgtt

Fig. 4B

3241 ttttaaaata tttatctgat taagttgtct aaacaatgct gatttggtga ccaactgtca
3301 ctcattgctg agcctctgct ccccagGGGA gttgtgtctg taatcgccct actattcagt
3361 ggcgagaaat aaagtttgct tagaaaagaa acatggtctc cttcttggaa ttaattctgc
3421 atctgcctct tcttgtgggt GGGAagaagc tccctaagtc ctctctccac aggctttaag
3481 atccctcgga cccagtccca tccttagact cctagggccc tggagaccct acataaacaa
3541 agcccaacag aatattcccc atccccccagg aaacaagagc ctgaacctaa ttacctctcc
3601 ctcagggcat GGGAatttcc aactctGGGA attc

Fig. 4C

Fig. 5A

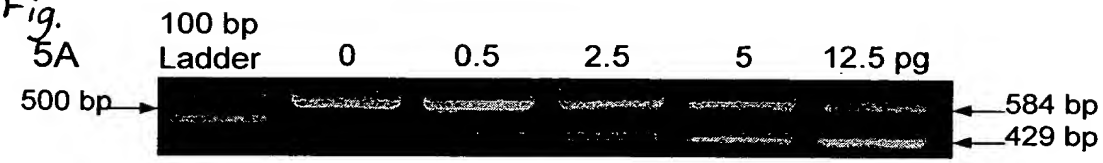


Fig. 5B

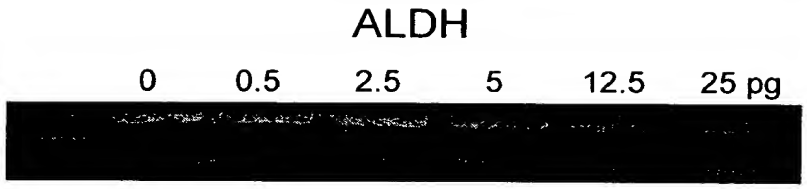


Fig. 5C

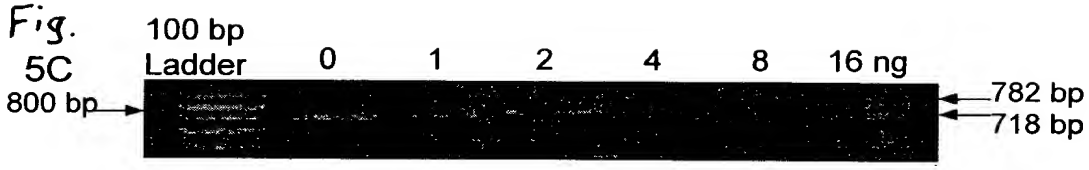


Fig. 5D

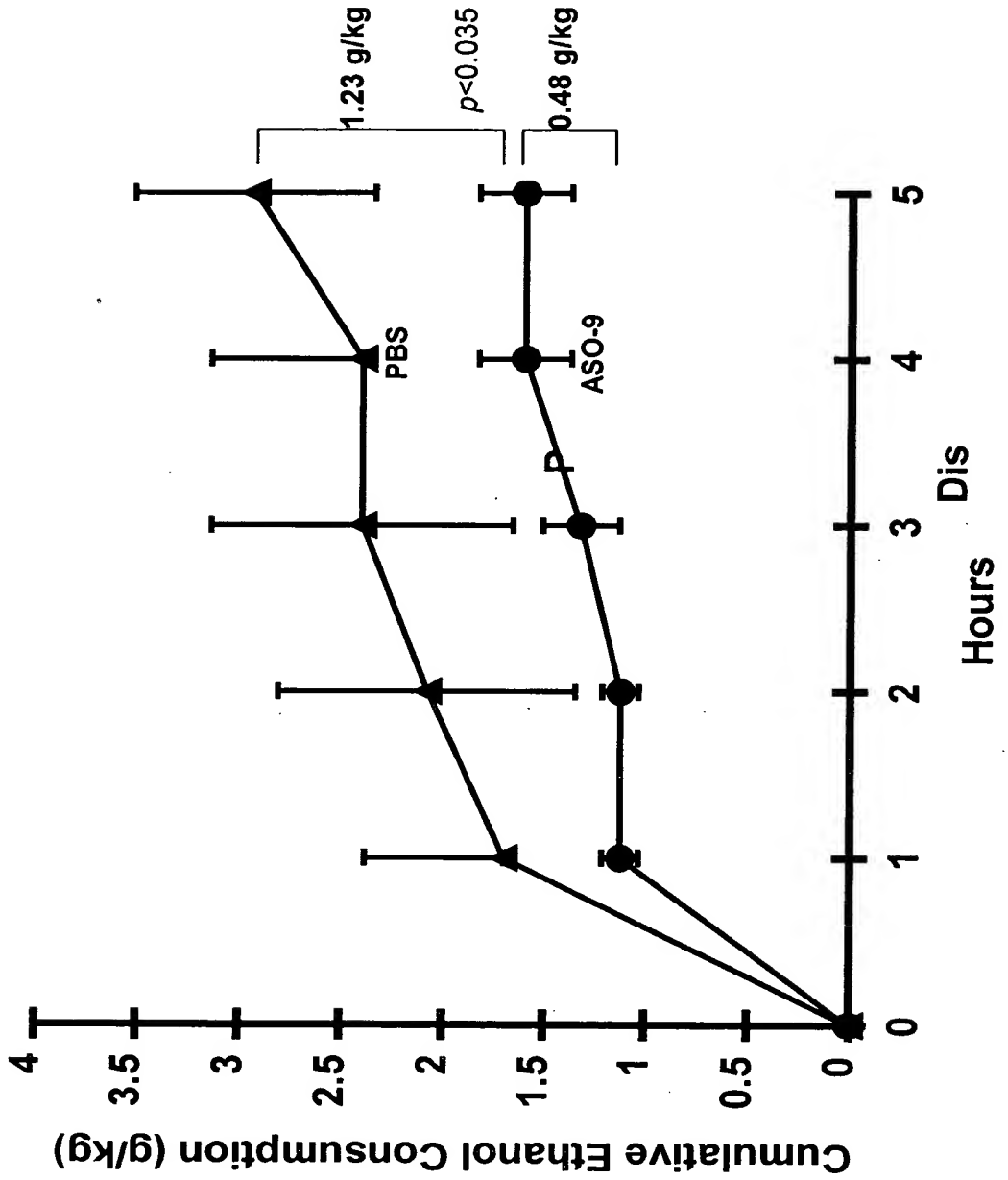

Cumulative Ethanol Consumption (g/kg)
0
0.5
1
1.5
2
2.5
3
3.5
4
0
1
2
3
4
5
Hours
Dis
PBS
ASO-9
P
1.23 g/kg
p<0.035
0.48 g/kg

FIGURE 6

Fig. 7A

Fig. 7B

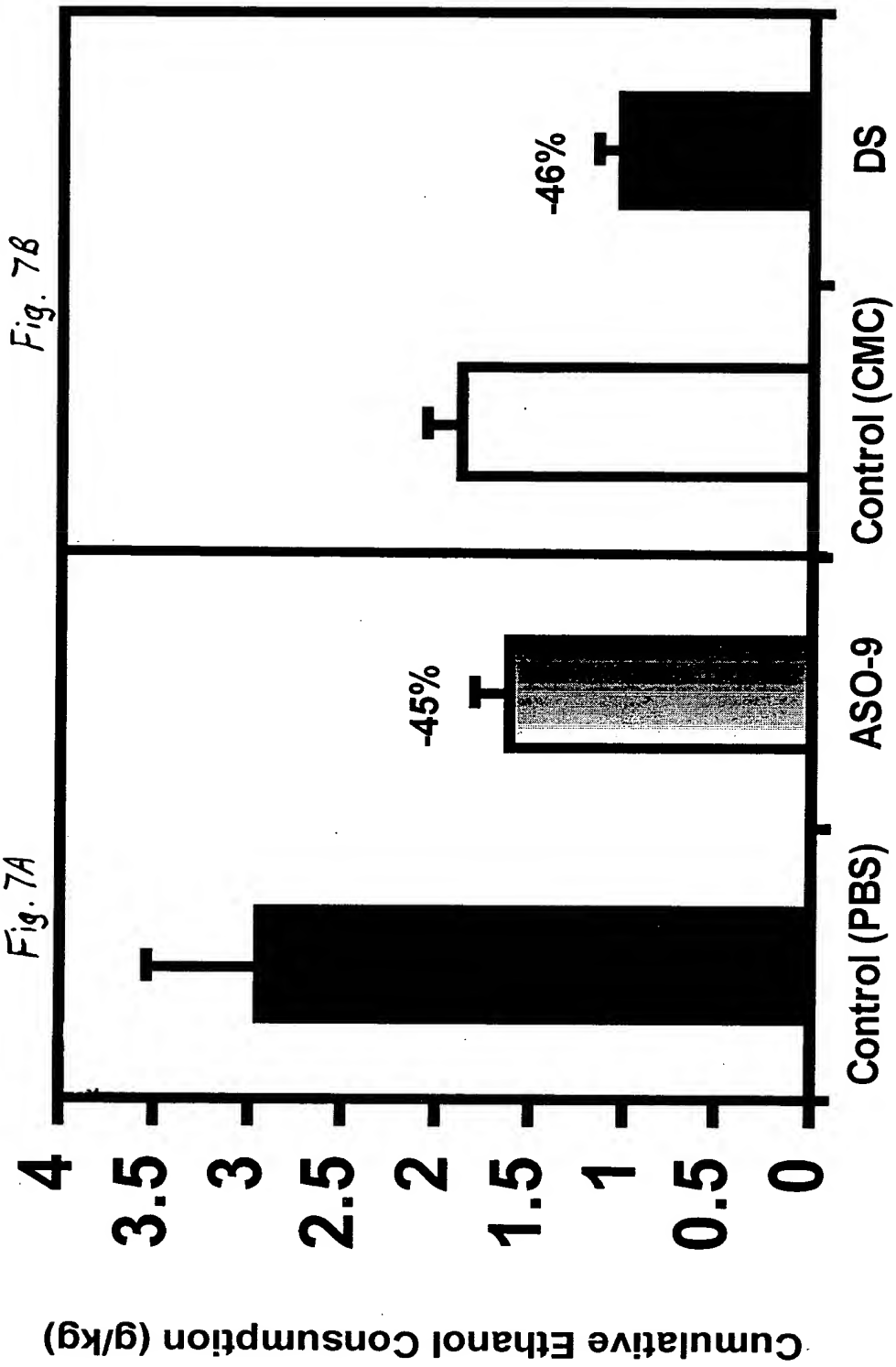

Cumulative Ethanol Consumption (g/kg)
4
3.5
3
2.5
2
1.5
1
0.5
0
Control (PBS)
ASO-9
Control (CMC)
DS
-45%
-46%

Fig. 8A

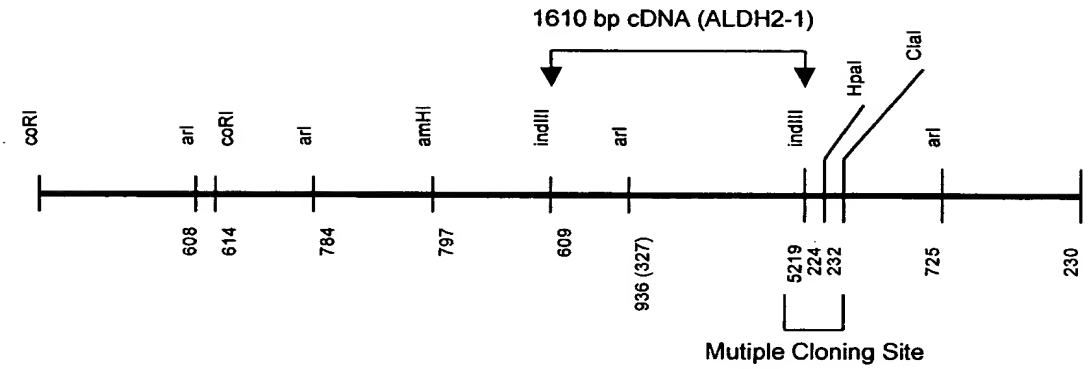

1610 bp cDNA (ALDH2-1)
HpaI
ClaI
coRI
arI
coRI
arI
amHI
indIII
arI
indIII
arI
608
614
784
797
609
936 (327)
5219
224
232
725
230
Mutiple Cloning Site

Fig. 8B

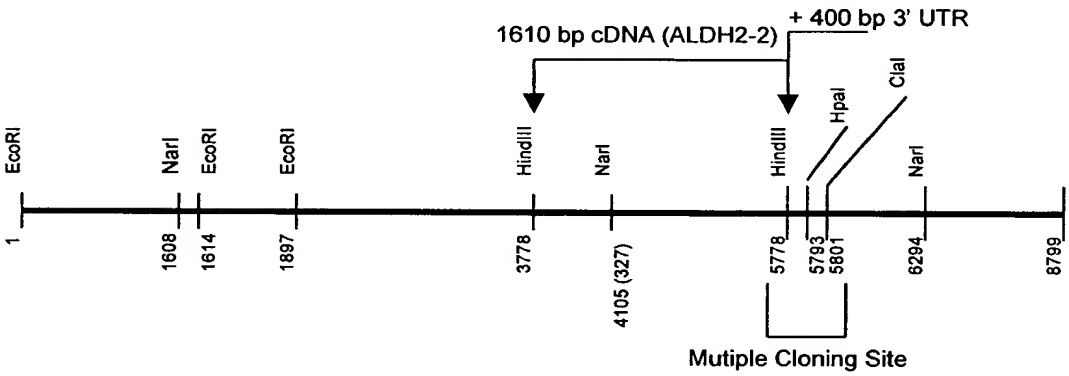

1610 bp cDNA (ALDH2-2)
+ 400 bp 3' UTR
HpaI
ClaI
EcoRI
NarI
EcoRI
EcoRI
HindIII
NarI
HindIII
NarI
1
1608
1614
1897
3778
4105 (327)
5778
5793
5801
6294
8799
Mutiple Cloning Site

FIGURE 9

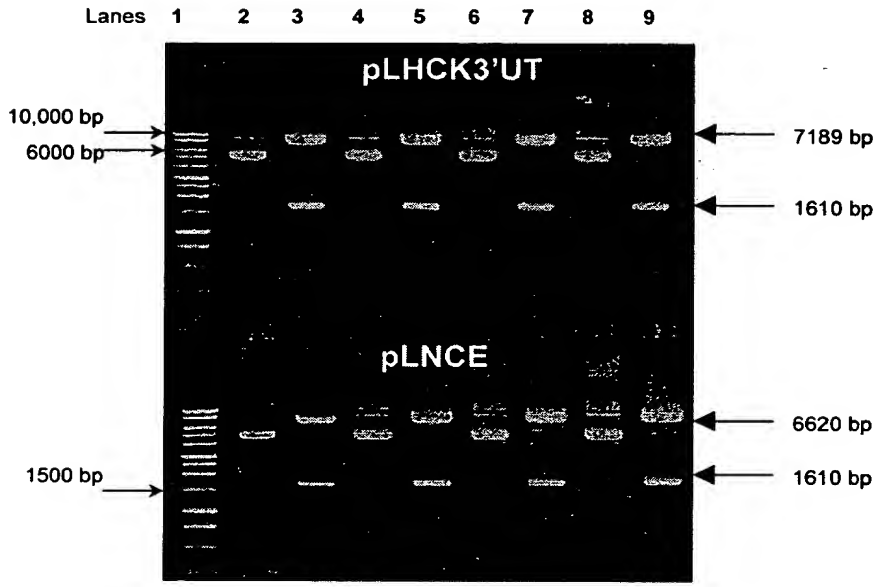
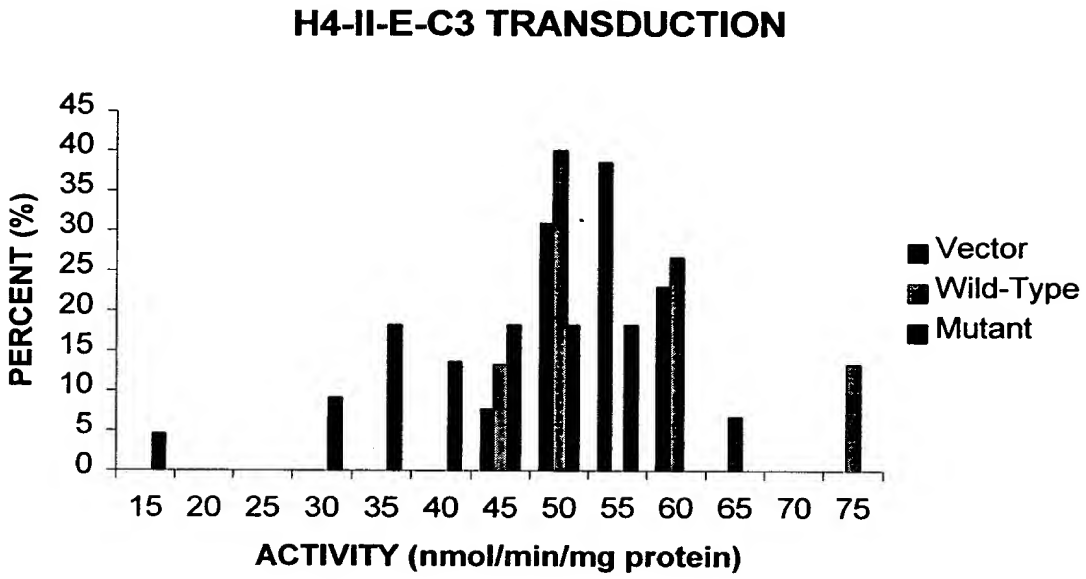

Lanes 1 2 3 4 5 6 7 8 9
pLHCK3'UT
10,000 bp
6000 bp
7189 bp
1610 bp
pLNCE
6620 bp
1500 bp
1610 bp

FIGURE 10


H4-II-E-C3 TRANSDUCTION
PERCENT (%)
45
40
35
30
25
20
15
10
5
0
15 20 25 30 35 40 45 50 55 60 65 70 75
ACTIVITY (nmol/min/mg protein)
Vector
Wild-Type
Mutant

GCTTTATCTG CTAAGCTCCG CTCAGTTCAG CATGCTGCGC GCCGCACTCA
GCACCGCCCG CCGTGGGCCA CGCCTGAGCC GCCTGCTGTC CGCCGCCGCC
ACCAGCGCGG TGCCAGCCCC CAACCAGCAG CCCGAGGTCT TCTGCAACCA
GATCTTCATT AACAATGAGT GGCATGATGC TGTCAGCAAG AAAACATTCC
CCACCGTCAA CCCTTCCACG GGGGAGGTCA TCTGCCAGGT AGCCGAAGGG
AACAAGGAGG ACGTAGACAA GGCAGTGAAG GCCGCTCAGG CAGCCTTCCA
GCTGGGCTCG CCCTGGCGCC GCATGGATGC ATCTGACAGG GGCCGGCTGT
TGTACCGATT GGCTGATCTC ATCGAACGGG ACCGGACCTA CCTGGCGGCC
TTGGAGACCC TGGACAACGG CAAGCCTTAT GTCATCTCCT ACCTGGTGGA
TTTGGACATG GTTCTGAAAT GTCTCCGCTA TTATGCTGGC TGGGCTGACA
AGTACCACGG GAAAACCATT CCCATCGATG GCGACTTCTT CAGCTACACC
CGCCACGAGC CTGTGGGCGT GTGTGGACAG ATCATTCCGT GGAACTTCCC
GCTCCTGATG CAAGCCTGGA AGCTGGGCCC TGCCTTGGCA ACTGGAAACG
TGGTGGTGAT GAAAGTGGCC GAGCAGACAC CGCTCACTGC ACTCTACGTG
GCCAACTTGA TCAAGGAGGC AGGCTTCCCC CCTGGTGTGG TCAATATTGT
TCCTGGATTC GGCCCTACCG CCGGGGCTGC CATCGCGTCC CACGAGGATG
TGGACAAAGT GGCCTTCACA GGTTCCACTG AGGTTGGTCA CCTAATCCAG
GTTGCCGCCG GGAGCAGCAA TCTCAAGAGA GTAACCCTGG AACTGGGGGG
AAAGAGCCCC AATATCATCA TGTCAGACGC TGACATGGAC TGGGCTGTGG
AACAGGCCCA CTTTGCCCTG TTCTTCAACC AGGGCCAGTG CTGTTGTGCG
GGCTCCCGGA CCTTCGTGCA GGAGGATGTG TATGATGAAT TCGTGGAACG
CAGTGTGGCC CGGGCCAAGT CTCGGGTGGT CGGGAACCCT TTCGACAGCC
GGACGGAGCA GGGGCCGCAG GTGGATGAGA CTCAGTTTAA GAAGATCCTG
GGCTATATCA AGTCAGGACA ACAAGAAGGG GCGAAGCTGC TGTGCGGTGG
GGGCGCCGCC GCAGACCGTG GTTACTTCAT CCAGCCCACC GTGTTCGGAG
ACGTCAAAGA TGGCATGACC ATCGCCAAGG AGGAGATCTT CGGACCAGTG
ATGCAGATCC TCAAATTCAA GACCATTGAG GAGGTTGTGG GGCGAGCCAA
TAATTCCAAG TACGGGCTGG CTGCCGCTGT CTTCACAAAG GACCTGGACA
AGGCCAATTA CCTGTCCCAA GCTCTGCAGG CTGGGACTGT GTGGATCAAC
TGCTACGATG TGTTTGGGGC CCAGTCCCCA TTTGGTGGCT ATAAGATGTC
GGGGAGCGGC AGGGAGCTGG GCGAGTATGG CCTGCAGGCC TACACGGAAG
TGAAGACGGT CACCGTCAAA GTGCCACAGA AGAACTCGTA AAGTGGCGTG
CAGGCTTCCT CAGCCAGCGC CCAAAAACCC AACAAGATCC TGAGAAAAGC
CACCACCAAG CACACTGCGC CTGCCAAGAG AAAACCCCTT CACCAAAGCG
TCTTGGGCCA AGAAAGTCAG GATTTGATAA ACAGGGCAGG GTTGGTGGGC
GGTGTGTGGG GAGCATCCCA GTAAACTGGG GAAGGGAGGA GCTCTGTGCA
GACTACCACG CGCACGCACA CACGCTCACT GGGTCCTTCT GTGCTGGATG
CTGGTTCCAC CCTCAGTGCT TAAACAAATG AGCAATAAA

Fig. 11

GCTCTCGGTC CGCTCGCTGT CCGCTAGCCC GCTGCGATGT TGCGCGCTGC
CGCCGCTCGG GCCCCGCCTG GCCGCCGCCT CTTGTCAGCC GCCGCCACCC
AGGCCGTGCC TGCCCCCAAC CAGCAGCCCG AGGTCTTCTG CAACCAGATT
TTCATAAACA ATGAATGGCA CGATGCCGTC AGCAGGAAAA CATTCCCCAC
CGTCAATCCG TCCACTGGAG AGGTCATCTG TCAGGTAGCT GAAGGGGACA
AGGAAGATGT GGACAAGGCA CGTGAAGGCC GCCCGGGCGC CTTCCAGCTG
GGCTCACCTT GGCGCCGCAT GGACGCATCA CACAGCGGCC GGCTGCTGAA
CCGCCTGGCC GATCTGATCG AGCGGGACCG GACCTACCTG GCGGCCTTGG
AGACCCTGGA CAATGGCAAG CCCTATGTCA TCTCCTACCT GGTGGATTTG
GACATGGTCC TCAAATGTCT CCGGTATTAT GCCGGCTGGG CTGATAAGTA
CCACGGGAAA ACCATCCCCA TTGACGGAGA CTTCTTCAGC TACACACGCC
ATGAACCTGT GGGGGTGTGC GGGCAGATCA TTCCGTGGAA TTTCCCGCTC
CTGATGCAAG CATGGAAGCT GGGCCCAGCC TTGGCAACTG GAAACGTGGT
TGTGATGAAG GTAGCTGAGC AGACACCCCT CACCGCCCTC TATGTGGCCA
ACCTGATCAA GGAGGCTGGC TTTCCCCCTG GTGTGGTCAA CATTGTGCCT
GGATTTGGCC CCACGGCTGG GGCCGCCATT GCCTCCCATG AGGATGTGGA
CAAAGTGGCA TTCACAGGCT CCACTGAGAT TGGCCGCGTA ATCCAGGTTG
CTGCTGGGAG CAGCAACCTC AAGAGAGTGA CCTTGGAGCT GGGGGGGAAG
AGCCCCAACA TCATCATGTC AGATGCCGAT ATGGATTGGG CCGTGGAACA
GGCCCACTTC GCCCTGTTCT TCAACCAGGG CCAGTGCTGC TGTGCCGGCT
CCCGGACCTT CGTGCAGGAG GACATCTATG ATGAGTTTGT GGTGCGGAGC
GTTGCCCGGG CCAAGTCTCG GGTGGTCGGG AACCCCTTTG ATAGCAAGAC
CGAGCAGGGG CCGCAGGTGG ATGAAACTCA GTTTAAGAAG ATCCTCGGCT
ACATCAACAC GGGGAAGCAA GAGGGGGCGA AGCTGCTGTG TGGTGGGGGC
ATTGCTGCTG ACCGTGGTTA CTTCATCCAG CCCACTGTGT TTGGAGATGT
GCAGGATGGC ATGACCATCG CCAAGGAGGA GATCTTCGGG CCAGTGATGC
AGATCCTGAA GTTCAAGACC ATAGAGGAGG TTGTTGGGAG AGCCAACAAT
TCCACGTACG GGCTGGCCGC AGCTGTCTTC ACAAAGGATT TGGACAAGGC
CAATTACCTG TCCCAGGCCC TCCAGGCGGG CACTGTGTGG GTCAACTGCT
ATGATGTGTT TGGAGCCCAG TCACCCTTTG GTGGCTACAA GATGTCGGGG
AGTGGCCGGG AGTTGGGCGA GTACGGGCTG CAGGCATACA CTGAAGTGAA
AACTGTCACA GTCAAAGTGC CTCAGAAGAA CTCATAAGAA TCATGCAAGC
TTCCTCCCTC AGCCATTGAT GGAAAGTTCA GCAAGATCAG CAACAAAACC
AAGAAAAATG ATCCTTGCGT GCTGAATATC TGAAAAGAGA AATTTTTCCT
ACAAAATCTC TTGGGTCAAG AAAGTTCTAG AATTTGAATT GATAAACATG
GTGGGTTGGC TGAGGGTAAG AGTATATGAG GAACCTTTTA AACGACAACA
ATACTGCTAG CTTTCAGGAT GATTTTTAAA AAATAGATTC AAATGTGTTA
TCCTCTCTCT GAAACGCTTC CTATAACTCG AGTTTATAGG GGAAGAAAAA
GCTATTGTTT ACAATTATAT CACCATTAAG GCAACTGCTA CACCCTGCTT
TGTATTCTGG GCTAAGATTC ATTAAAAACT AGCTGCTCT

Fig. 12